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**Roche Diagnostic Systems**

A Member of the Roche Group

Roche Diagnostic Systems, Inc.  
Branchburg Township  
1080 U.S. Highway 202  
Somerville, New Jersey 08876-3771

Direct Dial  
Fax

## **510(k) Summary**

### **Roche COBAS INTEGRA ISE Module Modification**

In accordance with the Safe Medical Devices Act of 1990, a 510(k) summary as outlined in 21 CFR 807.92 is provided herewith.

#### **I. Identification of 510(k) Sponsor:**

Roche Diagnostic Systems, Inc.  
a subsidiary of Hoffmann-La Roche, Inc.  
Branchburg Township  
1080 US Highway 202  
Somerville, NJ 08876-3771

510(k) Submission dated September 10, 1996

#### **II. Description of the Device/Statement of Intended Use:**

The COBAS INTEGRA test applications contained in this submission are intended for use with the COBAS INTEGRA Analyzer. The COBAS INTEGRA Analyzer and COBAS INTEGRA Reagent cassettes together provide an integrated system for *in vitro* diagnostic testing. The COBAS INTEGRA Analyzer along with 79 COBAS INTEGRA Reagent Cassettes were cleared on September 8, 1995 (K951595), January 25, 1996 (K954992) and July 23, 1996 (K961824). The COBAS INTEGRA Analyzer utilizes three measuring principles, i.e., absorbance, fluorescence polarization and ion-selective electrodes. The analyzer has a throughput of up to 600 tests per hour with STAT samples prioritized and tested immediately. Random sample access, robotics and a user interface optimize time management and streamline workflow. The COBAS INTEGRA can store up to 68 COBAS INTEGRA Reagent Cassettes on board, 24 hours a day at 2-8°C. The COBAS INTEGRA Reagent Cassettes are compact and preparation-free with

the added convenience of long term on-board stability. Barcode readers are used to identify newly loaded reagent cassettes, samples for patient identification, and rack inserts and to read calibration and control data from the cassette label. COBAS INTEGRA tests include chemistry, drugs of abuse, immunology, ion selective electrodes, therapeutic drug monitoring, and hematology reagents.

Through this submission, it is the intention of Roche Diagnostic Systems to gain clearance of a modified ISE Module which includes modified versions of the Direct Sodium, Direct Potassium, and Direct Chloride applications. These applications were previously cleared on September 8, 1995 (K951595). This premarket notification also includes new ISE applications for Direct Lithium, Indirect Sodium, Indirect Potassium, Indirect Chloride, Urine Sodium, Urine Potassium, and Urine Chloride.

The COBAS INTEGRA ISE module applications are intended for use for the quantitative determination of sodium, potassium, chloride, and lithium concentrations using ion-selective electrodes:

- the direct application is intended for undiluted serum and plasma
- the indirect application is intended for diluted serum and plasma (does not include lithium)
- the urine application is intended for diluted urine (does not include lithium)

### **III. Identification of the legally marketed device to which the 510(k) sponsor claims equivalence:**

The COBAS INTEGRA ISE Module applications are substantially equivalent to the corresponding applications for the Boehringer Mannheim / Hitachi 911 analyzer or the Kodak Ectachem 250 analyzer.

The ancillary reagents for the COBAS INTEGRA ISE Module were previously cleared in the original 510(k) for the ISE Module (K951595). However, ISE Solution 1 is now intended to be sold in two new packages with different names, "Calibrator Direct" and in a diluted form as "Calibrator Indirect/Urine". The new containers are larger and are stored on board the instrument, instead of using multiple vials of ISE Solution 1 in the ISE reagent rack.

The following table lists each ISE application and ancillary reagents with the corresponding predicate device or previously cleared device name.

**Table of Predicate Devices**

<b>Product Name</b>	<b>Predicate Product Name</b>	<b>K number</b>	<b>date of substantial equivalence</b>
<b>Roche COBAS INTEGRA ISE Module Tests:</b>			
Direct Sodium	BM / Hitachi 911 Sodium (Indirect)	K912648	07/17/91
Direct Potassium	BM / Hitachi 911 Potassium (Indirect)	K912649	07/15/91
Direct Chloride	BM / Hitachi 911 Chloride (Indirect)	K912647	07/17/91
Direct Lithium	Kodak Ectachem Lithium	K924488	01/26/93
Indirect Sodium	BM / Hitachi 911 Sodium (Indirect)	K912648	07/17/91
Indirect Potassium	BM / Hitachi 911 Potassium (Indirect)	K912649	07/15/91
Indirect Chloride	BM / Hitachi 911 Chloride (Indirect)	K912647	07/17/91
Urine Sodium	BM / Hitachi 911 Sodium (Urine)	K912648	07/17/91
Urine Potassium	BM / Hitachi 911 (Urine)	K912649	07/15/91
Urine Chloride	BM / Hitachi 911 (Urine)	K912647	07/17/91
<b>Roche COBAS INTEGRA ISE Module Ancillary Reagents</b>	<b>Previously approved Product Name</b>	<b>K Number</b>	<b>date of substantial equivalence</b>
ISE Solution 1	ISE Solution 1	K951595	09/08/95
ISE Solution 2	ISE Solution 2	K951595	09/08/95
ISE Solution 3	ISE Solution 3	K951595	09/08/95
ISE Calibrator Direct	ISE Solution 1	K951595	09/08/95
ISE Calibrator Indirect / Urine	ISE Solution 1 (diluted)	K951595	09/08/95

**IV. Summary of the technological characteristics of the new device in comparison to those of the predicate.**

A summary of the similarities, differences and performance characteristics between the COBAS INTEGRA ISE Module applications and the corresponding Boehringer Mannheim / Hitachi 911 or Kodak Ectachem 250 applications are listed in the following tables.

**Comparison Table - Direct Sodium**

	<b>COBAS INTEGRA Current ISE Direct Sodium Application</b>	<b>COBAS INTEGRA Modified ISE Direct Sodium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Sodium</b>
Intended Use	quantitative determination of sodium	quantitative determination of sodium	quantitative determination of sodium
Sample type	serum and plasma	serum and plasma	serum, plasma and urine
Methodology	Ion Selective Electrode - Direct	Ion Selective Electrode - Direct	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 150 mmol/L ISE Sol'n 2: 110 mmol/L	ISE Sol'n 1: 150 mmol/L ISE Sol'n 2: 110 mmol/L	STD 1: 120.0 mmol/L STD 2: 160.0 mmol/L
<b>Performance Characteristics:</b>			
Test Range	20 - 250 mmol/L		80 - 180 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	135.7    153.7	116        146	128.9    137.5    148.5
%CV (within run)	0.40      0.17	0.32      0.25	0.3       0.2       0.2
%CV (total)	1.1        1.6	1.0        0.69	0.5       0.4       0.6
Accuracy	y= 1.06x - 5.1 mmol/L r= 0.998   n=100 vs. BM / Hitachi 911	y= 0.99x + 5.3 mmol/L r= 0.989   n= 208 vs. BM / Hitachi 911	y= 1.018x - 2.35 mmol/L r= 0.999   n= 45 vs. flame photometry

**Comparison Table - Direct Potassium**

	<b>COBAS INTEGRA Current ISE Direct Potassium Application</b>	<b>COBAS INTEGRA Modified ISE Direct Potassium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Potassium</b>
Intended Use	quantitative determination of potassium	quantitative determination of potassium	quantitative determination of potassium
Sample type	serum and plasma	serum and plasma	serum and plasma
Methodology	Ion Selective Electrode - Direct	Ion Selective Electrode - Direct	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 5 mmol/L ISE Sol'n 2: 1.8 mmol/L	ISE Sol'n 1: 5 mmol/L ISE Sol'n 2: 1.8 mmol/L	STD 1: 3.00 mmol/L STD 2: 7.00 mmol/L
<b>Performance Characteristics:</b>			
Test Range	0.2 - 30 mmol/L		1.5 - 10.0 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	3.18       7.25	4.3        7.2	3.41       5.69       6.40
%CV (within run)	0.30       0.42	0.24       0.29	0.3        0.2        0.3
%CV (total)	1.5        1.8	0.75       0.89	0.7        0.5        0.7
Accuracy	y= 1.07x - 0.22 mmol/L r= 0.999   n=100 vs. BM / Hitachi 911	y= 1.03x + 0.02 mmol/L r= 0.998   n= 208 vs. BM / Hitachi 911	y= 1.041x - 0.177 mmol/L r= 0.999   n= 52 vs. flame photometry

**Comparison Table - Direct Chloride**

	<b>COBAS INTEGRA Current ISE Direct Chloride Application</b>	<b>COBAS INTEGRA Modified ISE Direct Chloride Application</b>	<b>Boehringer Mannheim/Hitachi 911 Chloride</b>
Intended Use	quantitative determination of chloride	quantitative determination of chloride	quantitative determination of chloride
Sample type	serum and plasma	serum and plasma	serum, and urine
Methodology	Ion Selective Electrode - Direct	Ion Selective Electrode - Direct	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 115 mmol/L ISE Sol'n 2: 72 mmol/L	ISE Sol'n 1: 115 mmol/L ISE Sol'n 2: 72 mmol/L	STD 1: 80.0 mmol/L STD 2: 120.0 mmol/L
<b>Performance Characteristics:</b>			
Test Range	20 - 250 mmol/L	20 - 250 mmol/L	60 - 140 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	135.7    153.7	92        106	89.2    102.2    113.7
%CV (within run)	0.40    0.17	0.39    0.37	0.4      0.3      0.3
%CV (total)	1.1      1.6	1.3      0.85	0.7      0.5      0.8
Accuracy	$y = 1.19x - 17.9$ mmol/L $r = 0.996$ $n = 100$ vs. BM / Hitachi 911	$y = 0.91x + 12.8$ mmol/L $r = 0.969$ $n = 208$ vs. BM / Hitachi 911	$y = 1.073x - 8.80$ mmol/L $r = 0.999$ $n = 42$ vs. chloridometer

**Comparison Table - Direct Lithium**

	<b>COBAS INTEGRA ISE Direct Lithium Application</b>	<b>Kodak Ectachem Lithium</b>
Intended Use	quantitative determination of lithium	quantitative determination of lithium
Sample type	serum and plasma	serum and plasma
Methodology	Ion Selective Electrode - Direct	Colorimetric
Standards	ISE Sol'n 1: 0.3 mmol/L ISE Sol'n 2: 0.3 mmol/L ISE Sol'n 3: 1.4 mmol/L	information not available
<b>Performance Characteristics:</b>		
Test Range	0.1 - 4 mmol/L	0.20 - 4.00 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3    Level 4
Mean (mmol/L)	0.44      1.9	0.47    0.96    1.17    2.14
%CV (total)	3.4        2.9	6.93    4.76    3.86    3.12
Accuracy	$y = 0.98x - 0.10$ mmol/L $r = 0.964$ $n = 244$ vs. Kodak Ectachem	$y = 1.00x - 0.03$ mmol/L $r = 0.991$ $n = 200$ vs. ion-selective electrode

**Comparison Table - Indirect Sodium**

	<b>COBAS INTEGRA Modified ISE Indirect Sodium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Sodium</b>
Intended Use	quantitative determination of sodium	quantitative determination of sodium
Sample type	serum and plasma	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 150 mmol/L ISE Sol'n 2: 110 mmol/L	STD 1: 120.0 mmol/L STD 2: 160.0 mmol/L
<b>Performance Characteristics:</b>		
Test Range	20 - 250 mmol/L	80 - 180 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	112        138	128.9    137.5    148.5
%CV (within run)	0.26       0.24	0.3       0.2       0.2
%CV (total)	1.0        0.59	0.5       0.4       0.6
Accuracy	$y = 0.96x - 1.2$ mmol/L $r = 0.994$ $n = 208$ vs. BM / Hitachi 911	$y = 1.018x - 2.35$ mmol/L $r = 0.999$ $n = 45$ vs. flame photometry

**Comparison Table - Indirect Potassium**

	<b>COBAS INTEGRA ISE Indirect Potassium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Potassium</b>
Intended Use	quantitative determination of potassium	quantitative determination of potassium
Sample type	serum and plasma	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 5 mmol/L ISE Sol'n 2: 1.8 mmol/L	STD 1: 3.00 mmol/L STD 2: 7.00 mmol/L
<b>Performance Characteristics:</b>		
Test Range	0.2 - 30 mmol/L	1.5 - 10.0 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	4.3        6.9	3.41    5.69    6.40
%CV (within run)	0.44       0.31	0.3       0.2       0.3
%CV (total)	0.75       0.83	0.7       0.5       0.7
Accuracy	$y = 1.00x - 0.09$ mmol/L $r = 0.999$ $n = 208$ vs. BM / Hitachi 911	$y = 1.041x - 0.177$ mmol/L $r = 0.999$ $n = 52$ vs. flame photometry

**Comparison Table - Indirect Chloride**

	<b>COBAS INTEGRA ISE Indirect Chloride Application</b>	<b>Boehringer Mannheim/Hitachi 911 Chloride</b>
Intended Use	quantitative determination of chloride	quantitative determination of chloride
Sample type	serum and plasma	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 115 mmol/L ISE Sol'n 2: 72 mmol/L	STD 1: 80.0 mmol/L STD 2: 120.0 mmol/L
<b>Performance Characteristics:</b>		
Test Range	20 - 250 mmol/L	60 - 140 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	92            107	89.2        102.2      113.7
%CV (within run)	0.36        0.26	0.4          0.3        0.3
%CV (total)	1.1          0.83	0.7          0.5        0.8
Accuracy	$y = 0.90x + 11.1$ mmol/L $r = 0.980$ $n = 208$ vs. BM / Hitachi 911	$y = 1.073x - 8.80$ mmol/L $r = 0.999$ $n = 42$ vs. chloridometer

**Comparison Table - Urine Sodium**

	<b>COBAS INTEGRA ISE Urine Sodium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Sodium</b>
Intended Use	quantitative determination of sodium	quantitative determination of sodium
Sample type	urine	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 150 mmol/L ISE Sol'n 2: 110 mmol/L	STD 1: 120.0 mmol/L STD 2: 160.0 mmol/L
<b>Performance Characteristics:</b>		
Test Range	20 - 350 mmol/L	10 - 250 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	56            259	58.3        107.2      177.4
%CV (within run)	1.0           0.49	0.4          0.3        0.3
%CV (total)	3.0           1.2	1.0          0.6        0.6
Accuracy	$y = 0.95x + 3.4$ mmol/L $r = 0.996$ $n = 174$ vs. BM / Hitachi 911	$y = 0.963x + 3.06$ $r = 1.000$ $n = 49$ vs. flame photometry

**Comparison Table - Urine Potassium**

	<b>COBAS INTEGRA ISE Urine Potassium Application</b>	<b>Boehringer Mannheim/Hitachi 911 Potassium</b>
Intended Use	quantitative determination of potassium	quantitative determination of potassium
Sample type	urine	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 5 mmol/L ISE Sol'n 2: 1.8 mmol/L	STD 1: 3.00 mmol/L STD 2: 7.00 mmol/L
<b>Performance Characteristics:</b>		
Test Range	1 - 150 mmol/L	1.5 - 80 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	33            125	22.9        44.1        69.5
%CV (within run)	0.26        0.67	0.4          0.7          0.9
%CV (total)	1.4          2.0	0.8          1.1          1.6
Accuracy	$y = 1.04x - 0.7$ mmol/L $r = 0.999$ $n = 162$ vs. BM / Hitachi 911	$y = 1.035x + 1.45$ $r = 0.999$ $n = 42$ vs. flame photometry

**Comparison Table - Urine Chloride**

	<b>COBAS INTEGRA ISE Urine Chloride Application</b>	<b>Boehringer Mannheim/Hitachi 911 Chloride</b>
Intended Use	quantitative determination of chloride	quantitative determination of chloride
Sample type	urine	serum, plasma and urine
Methodology	Ion Selective Electrode - Indirect	Ion Selective Electrode - Indirect
Standards	ISE Sol'n 1: 115 mmol/L ISE Sol'n 2: 72 mmol/L	STD 1: 80.0 mmol/L STD 2: 120.0 mmol/L
<b>Performance Characteristics:</b>		
Test Range	20 - 350 mmol/L	1.5 - 80 mmol/L
Precision:	Level 1    Level 2	Level 1    Level 2    Level 3
Mean (mmol/L)	147            274	50.3        122.5        202.0
%CV (within run)	0.44        0.30	0.7          0.7          0.6
%CV (total)	1.1          2.1	1.6          0.9          1.2
Accuracy	$y = 0.95x + 11.0$ mmol/L $r = 0.981$ $n = 164$ vs. BM / Hitachi 911	$y = 1.033x - 3.08$ $r = 0.996$ $n = 41$ vs. flame photometry



**V. Breif discussion of the clinical and nonclinical tests relied on for a determination of substantial equivalence:**

To demonstrate equivalence in performance characteristics, the COBAS INTEGRA ISE Module applications were tested for precision and accuracy. See tables in previous section for results.

*Precision Study*

Precision was evaluated using two levels of controls following the guidelines from NCCLS EP5-T2.

*Correlation Study*

Correlation studies were done comparing the Sodium, Potassium, Chloride, and Lithium applications with the corresponding applications on the Boehringer Mannheim / Hitachi 911 analyzer and Lithium with the Kodak Ectachem 250 application. Greater than 200 specimens were tested on both systems for each application. The results were evaluated using linear regression analysis.